Key Considerations and Strategies for Strengthening Covid-19 Diagnostics

Supply Chains in Low- and Middle-Income Country Settings

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msh Management Sciences for Health

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Abbreviations

Ab	antibody
ACT	Accelerator Covid-19 Tools initiative
Ag	antigen
AIDS	acquired immumondeficiency syndrome
AMDF	Africa Medical Devices Forum
ASSURED	Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment-free and Deliverable to end-users
CDC	US Centers for Disease Control and Prevention
Covid-19	coronavirus disease 2019
CSCS	Covid-19 Supply Chain System
DNA	deoxyribonucleic acid
ELISA	enzyme-linked immunosorbent assay
EMA	European Medicines Agency
EOC	emergency operations center
EUA	emergency use authorization
EUL	Emergency Use Listing (WHO)
FDA	Food and Drug Administration
FIND	Foundation for Innovative New Diagnostics
GBT	global benchmarking tool
HIV	human immunodeficiency virus
HTA	health technology assessment
IHR	International Health Regulations
IVD	in vitro diagnostic
LMICs	low- and middle-income countries
MERS	Middle East respiratory syndrome
MSH	Management Sciences for Health
MTaPS	Medicines, Technologies, and Pharmaceutical Services
NRA	national regulatory authority
PACT	Partnership to Accelerate Covid-19 Testing (PACT) in Africa
PAN	Pandemic Action Network
POC	point of care
PCR	polymerase chain reaction
PPE	personal protective equipment
RDT	rapid diagnostic test
RT-PCR	reverse transcripase–polymerase chain reaction
SARS–CoV-2	severe acute respiratory syndrome coronavirus-2
UN	United Nations
UNICEF	United Nations Children's Fund
USAID	US Agency for International Development
WHO	World Health Organization

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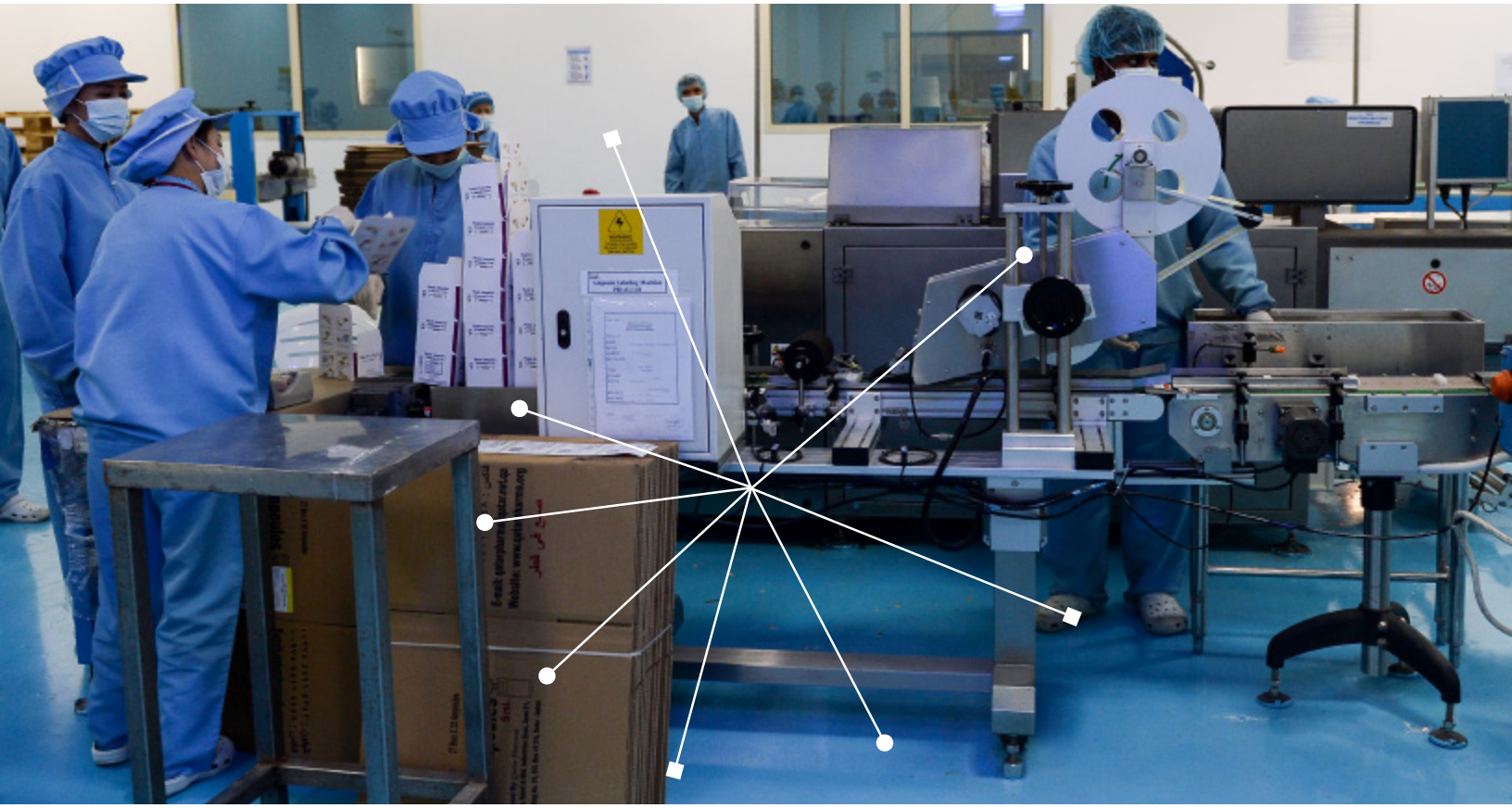
This document was developed by a multidisciplinary team at MSH. Kwesi Eghan and Ritu Kumar led the research and analysis. Andualem Oumer, Emmanuel Nfor, Francis Aboagye-Nyame, and Javier Guzman provided additional technical inputs and review of the document. The project team was led by Dr. Hector Castro, who provided overall direction and design for the project. With this document we aim to support LMICs in rational selection, and deployment of diagnostics for Covid-19.

The scope of this landscape analysis is limited to molecular, antigen, and antibody diagnostic devices to detect COVID -19 infection. The information presented in the analysis and dashboard has been verified via triangulation between secondary data sources and supplemental key informant interviews. However, the analysis in the report is not exhaustive of all available tests in the market since it is focused on tests that are suitable for LMIC needs. This includes tests that leverage existing PCR platforms and tests that have been introduced through global pooled procurement initiatives. All efforts have been made to ensure that the report provides an accurate overview of the listed Covid-19 diagnostics. However, the landscape for Covid-19 diagnostics is rapidly changing and additional devices entering the market after the completion of the report may not be included, and information supplied concerning the identified tests may change rapidly or vary by geography.



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Executive Summary

Diagnostics and testing are a cornerstone of the management and control of the ongoing coronavirus disease (Covid-19) pandemic. Detection of cases and isolation of infected individuals are critical to interrupt disease transmission. The global demand for diagnostics, reagents, and consumables for Covid-19 is causing shortages of commodities. The shortages have considerable impact on LMICs, which are significantly resource-constrained and lack the political clout to secure supplies. Awareness and assessment of the potential bottlenecks are critical for countries to mitigate the risks and secure the supply of the appropriate diagnostics. The *Key Considerations and Strategies for Strengthening Covid-19 Diagnostics Supply Chains in Low- and Middle-Income Country Settings* document outlines the major challenges and potential mitigation strategies to support LMICs in securing access to appropriate, quality-assured, and adequate Covid-19 diagnostics.

The document starts by providing an overview of crucial strategic planning structures and processes that are needed for an effective pandemic response. Types of tests, recommended testing strategies, and potential trade-offs are outlined within the following section. The document expands upon challenges and mitigation strategies related to regulatory, demand planning, procurement, and distribution of Covid-19 diagnostics. The financing and budgeting section provides insight into considerations for management of constrained resources. Guidelines, frameworks, and tools for decision support are referenced throughout the document for ease of access. The overall aim is to support the evidence-based selection and deployment of diagnostics for Covid-19 in low- and middle-income countries.

1. Purpose of Guidance Document

Covid-19 has become a global challenge, with infections spread across 216 countries and territories as of September 2020. Testing to detect, trace, and isolate individuals infected or exposed to SARS-CoV-2 is crucial to management and mitigation of the pandemic. This has led to an immense demand for diagnostics, reagents, and consumables for Covid-19, which is causing global shortages for these commodities. The impact of shortages has been magnified in LMICs, which face preexisting challenges of limited resources and vulnerable health systems. Global and regional collaboration initiatives such as Accelerator Covid-19 Tools (ACT), Pandemic Action Network (PAN), and Partnership to Accelerate Covid-19 Testing (PACT) in Africa have emerged to support LMICs in addressing these challenges. Given the growing number of global infections, however, countries will continue to face significant challenges in scaling up and sustaining testing. This document, *Key Considerations and Strategies for Strengthening Covid-19 Diagnostics Supply Chains in Low- and Middle-Income Country Settings,* has been developed to assist resource-constrained settings in anticipating and responding to the current supply challenges for diagnostics.

Aims and Objectives: This document has been developed to describe the challenges facing LMICs in accessing appropriate, quality-assured, and adequate Covid-19 diagnostics and potential strategies for mitigating these challenges. This guidance document is a companion document to a landscape analysis and dashboard of available tests worldwide, developed to support the rational selection of these tests appropriate to the context in LMICs.

Target Audience: Targeted users include policy makers involved in Covid-19 response in LMICs, personnel from ministries of health, laboratory managers and technicians, other health professionals engaged in Covid-19 response, and not-for-profit organizations, donors, and international agencies supporting LMICs' Covid-19 response. Together, this guidance document, the landscape analysis, and the dashboard address the public-sector response to Covid-19, are specifically intended for officials who make decisions about deployment and procurement of laboratory tests and equipment.

2. Strategic Planning and Coordination

2.1 Background

Over the last decade, the world has observed several epidemic outbreaks, including severe acute respiratory syndrome, H1N1 influenza, Middle East respiratory syndrome, and Ebola virus disease. The current coronavirus disease pandemic has emerged as one of the most significant pandemics in recent history. Covid-19 is a highly contagious infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease spreads through small droplets that are released when an infected individual coughs, sneezes, or speaks. It can also be passed on indirectly when a person comes into contact with surfaces contaminated by the virus.

There is increasing recognition that, given the recurrent nature of epidemics, it is crucial to build resilient health systems and improve national pandemic preparedness. World Health Organization (WHO) member states came together in 2005 to create the International Health Regulations (IHR), an international legal and operational framework for the response to global public health emergencies. The IHR require that all countries build the capacity to detect, assess, report, and respond to public health emergencies such as pandemics.

Diagnostics are vital for each stage of addressing the disease: (1) detection of the disease; (2) assessing and reporting the spread of the disease and associated risks; and (3) response to the disease, including infection prevention and control, mitigation, and recovery. Because, however, Covid-19 has become a global challenge with infections spread across 216 countries and territories, there is a global shortage of diagnostics, reagents, and consumables as all countries respond to the epidemic. The impact of shortages is especially acute in LMICs, which face preexisting challenges of limited resources and vulnerable health systems.

Several global and regional collaboration initiatives have emerged to support LMICs in obtaining access to the commodities needed to tackle the pandemic. Initiatives such ACT, PAN, and PACT in African LMICs have helped advocate for fund mobilization, the streamlining of supply chains, and encouraging manufacturers to increase production of laboratory supplies. Given the growing number of infections and ongoing shortages, however, a set of practical and nuanced strategies is needed for response. This document has been developed to assist LMICs in anticipating and responding to the current supply challenges for diagnostics.

2.2 Assumptions and Considerations for Developing this Document

Given the several epidemic outbreaks in the recent past and that 196 countries have signed on to the IHR, this document assumes the existence of a baseline set of pandemic response protocols and management structures. WHO's Pandemic Preparedness Framework (2013) provides foundational guidance to LMICs in strengthening plans and procedures for responding to the ongoing Covid-19 pandemic. WHO's guidance provides the crucial steps based on which LMICs can tailor their national responses for the local context. This document assumes that countries have already established a national emergency response mechanism such as an emergency operations center (EOC) with the legal and policy mandate to manage the Covid-19 response, including:

1. Country-level coordination, planning, and monitoring
2. Risk communication and community engagement

3. Surveillance, rapid-response teams, and case investigation
4. Points of entry, international travel, and transport
5. National laboratories
6. Infection prevention and control
7. Case management
8. Operational support and logistics
9. Maintaining essential health services and systems

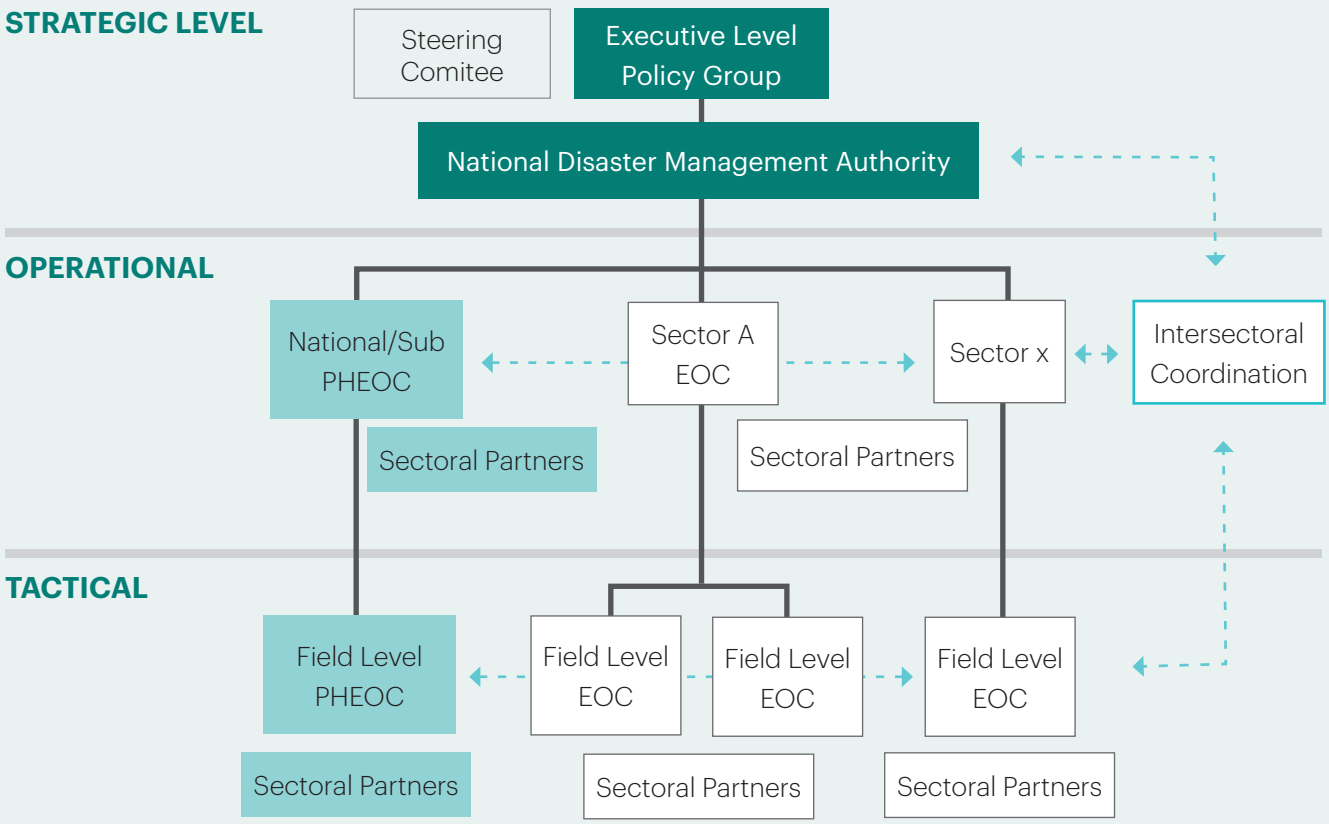
Additionally, this guidance document takes into consideration the following aspects that governments face in addressing the pandemic (adapted from WHO's *Novel Coronavirus (2019–nCoV): Strategic Preparedness and Response Plan*):

1. Minimizing disease transmission, including preventing large-scale spread as much as possible
2. Identifying, isolating, and providing necessary care for patients as early as possible
3. Monitoring and assessing the spread and impact of the disease for their local context and demographics—especially as there are still many unknowns about Covid-19
4. Ensuring availability of treatments and diagnostics
5. Communicating and countering misinformation about the pandemic to all communities
6. Minimizing social and economic impact—this is especially important in the context of LMICs with limited resources for social security and significant low-income populations who face catastrophic consequences if placed under lockdown for long periods

Pandemic Management Organizational Structures

A mechanism such as an EOC will consist of a multisectoral team in charge of developing, operationalizing, implementing, monitoring, and updating the strategies for combating the pandemic. Teams and structures would need to exist at national/subnational and functional levels, including one focused on laboratory response. WHO's *Framework for a Public Health Emergency Operations Centre* provides an example of a potential organizational structure, as shown in figure 1.

Figure 1. Public health emergency operations management structure, WHO



Source: WHO Framework for a Public Health Emergency Operations Centre. November 2015

The functional pandemic response mechanism for laboratory response should include developing and implementing protocols for selecting, sourcing, distributing, and maintaining diagnostics for Covid-19. WHO's *Operational Planning Guidelines to Support Country Preparedness and Response* provide the foundational elements for national laboratory strategies for LMICs, as shown in figure 2.

Figure 2. WHO's action/checklist to prepare laboratory capacity for large-scale testing

Step	Actions to be taken
1.	☐ Establish access to designated domestic Covid-19 diagnostic laboratory(ies) through public , private and academic systems, and consider use of veterinary laboratories
	☐ Adopt and disseminate SOPs (as part of disease outbreak investigation protocols) for collection, management, and transport of Covid-19 diagnostic specimens
	☐ Identify hazards and perform a biosafety risk assessment at designated laboratories; use appropriate biosafety measures to mitigate risks
	☐ Laboratories should adopt systems for molecular (PCR) testing, supported by timely access to reagents, testing kits, and a trained workforce
2.	☐ Ensure specimen collection, management, referral network and procedures are functional
	☐ Share genetic sequence data and virus materials according to established protocols for Covid-19
	☐ Develop and implement plans to link laboratory data with other key epidemiological data for timely data analysis
	☐ Develop and implement surge plans to manage increased demand for testing; consider conservation of lab resources in anticipation of potential widespread COYID-19 transmission
3.	☐ Monitor and evaluate diagnostics, data quality and staff performance, including use of and performance with different platforms, and incorporate findings into a strategic review of national laboratary capacity; share lessons learned
	☐ Develop a quality assurance mechanism for laboratory testing, including quality indicators

Source: WHO's Operational Planning Guidelines to Support Country Preparedness and Response

WHO's guidance provides a solid foundation for countries, but its implementation will differ based on each country's needs. Timely diagnosis is key to minimizing the spread and impact of Covid-19; therefore, LMICs must leverage laboratory capacities across private, public, and academic sectors to maximize access to testing.

2.3 Types of Tests

The main type of tests available for Covid-19 testing are the following:

- **RT-PCR tests.** These are nucleic acid amplification tests (NAATs) that detect viral RNA in patient samples from the upper and lower respiratory tract (e.g., nasal or oropharyngeal swabs, sputum, or bronchial lavage) to diagnose and/or confirm cases. The diagnostic tests rely on a technique called reverse transcriptase–polymerase chain reaction (RT-PCR) to detect the presence of SARS-CoV-2 virus. These tests can provide qualitative results (meaning positive or negative findings) as well as quantitative information on the amount of circulating virus in a patient sample. These assays have high analytical sensitivity, with an estimated limit of detection ranging from 100–1,000 copies, and very high specificity. These are currently considered the gold standard in Covid-19 diagnostics.
- **Antigen (Ag) tests.** These are used to detect viral proteins in samples from both the upper and lower respiratory tract and can be used from 1 to 14 days post–onset of symptoms. They have a high variability in terms of accuracy when compared with RT-PCR tests.
- **Serological or "antibody" tests.** These detect evidence of the body's immune response to an infection, which can provide information on both current and prior infection. Serological tests make

it possible to detect infections after the immune system has successfully eliminated the pathogen. These include rapid diagnostic tests (RDTs) that rely on a biological sample (e.g., blood, urine), which is placed on a *lateral flow immunassay* (LFIA) test strip, which returns qualitative (positive or negative) results within minutes. These also include *enzyme-linked immunosorbent assays (ELISAs),* which rely on specific binding of patient antibodies to a fixed viral protein of interest. ELISAs can return qualitative or quantitative results and are generally performed in a lab setting. These tests use whole blood, plasma, or serum samples; patient samples need to be incubated with the viral protein of interest. *Neutralization assays,* are another type of antibody (Ab) test, which provide quantitative information on the ability of a patient's antibody to confer protective immunity. Neutralization assays are the most resource-intense (time-consuming and skills-based) of the three antibody tests types described. These tests require whole blood, serum, or plasma samples from the patient. The test entails cell culture with the live virus and patient samples.

Currently, WHO and the US Centers for Disease Control and Prevention (CDC) do not recommend using antigen or Ab testing as the sole basis for diagnosis of infection. WHO recommends using antibody tests only for epidemiological research and assessing them for surveillance. In the case of Ag testing, WHO has recommended waiting for accurate validation results of key tests before widespread use. The Africa Centers for Disease Control and Prevention (CDC) recommends using Ab testing for triaging and testing confirmed contacts of Covid-19 cases.

The information in this section provides an overview of the available tests. For more detailed information, please refer to the companion document, *A Landscape Analysis of Laboratory Technologies for Covid-19 Response in Low- and Middle-Income Countries: Equipment, Reagents, and Supplies for Diagnostic Molecular, Antigen, and Serological Testing*.

2.4 Testing Strategies

SARS-CoV-2 is a novel coronavirus. The global knowledge base about its characteristics and impact is highly dynamic and growing quickly. Countries' response strategies, including those for testing for the virus, need to be continually updated. The selection, quantification, purchase, distribution, and use of tests will depend on the testing strategies being adopted by the country. Various global organizations have provided guidance on test strategies, which can serve as a useful base that LMICs can tailor to their specific needs. Some of these strategies are described below.

World Health Organization. WHO has defined four transmission scenarios and corresponding testing approaches. Further described in table 1, these are:

1. Number of cases: number of reported cases
2. Sporadic cases: one or more cases imported or locally acquired
3. Clusters of cases: most cases of transmission linked to chains of transmission
4. Community transmission: outbreaks with the inability to relate confirmed cases through chains of transmission for a large number of cases OR increasing positive tests through sentinel samples (routine systematic testing of respiratory samples from established laboratories)

Table 1. WHO's recommended testing approaches based on transmission scenario

	No. cases	Sporadic cases	Clusters of cases	Community transmission
Testing approach	Test all cases meeting suspect case definition; test patients with unexpected clinical presentation or where there is an increase in hospital admissions in a specific demographic group that could be Covid-19; test samples for surveillance from severe acute respiratory illness (SARI) or influenza like illness (ILI).	Test all cases meeting suspect case definition; test samples for surveillance from SARI or ILI.	Test all cases meeting suspect case definition; test samples for surveillance from SARI or ILI.	If diagnostic capacity is insufficient, implement prioritized testing and measures that can reduce spread (e.g., isolation), including priority testing of: - People at risk of developing severe disease and vulnerable populations, who will require hospitalization and advanced care for Covid-19 - Health workers (including emergency services and nonclinical staff) regardless of whether they are a contact of a confirmed case (to protect health workers and reduce the risk of nosocomial transmission) - The first symptomatic individuals in a closed setting (e.g., schools, long-term living facilities, prisons, hospitals). or fragile settings (e.g., humanitarian operations, refugee/migrant camp and non-camp settings) to quickly identify outbreaks and ensure containment measures.

Source: WHO Laboratory testing strategy recommendations for Covid-19 March 2020

Africa Centers for Disease Control. Africa CDC issued guidance on the use of rapid antibody tests due to the challenges of access to molecular tests (the gold standard) and increasing availability of a number of rapid antibody tests for Covid-19. While rapid antibody tests can be an important part of country testing strategies, there is limited validation of most of them for quality and accuracy. Therefore, rapid tests need to be used thoughtfully to prevent wastage of limited resources. At this point, the Africa CDC recommends:

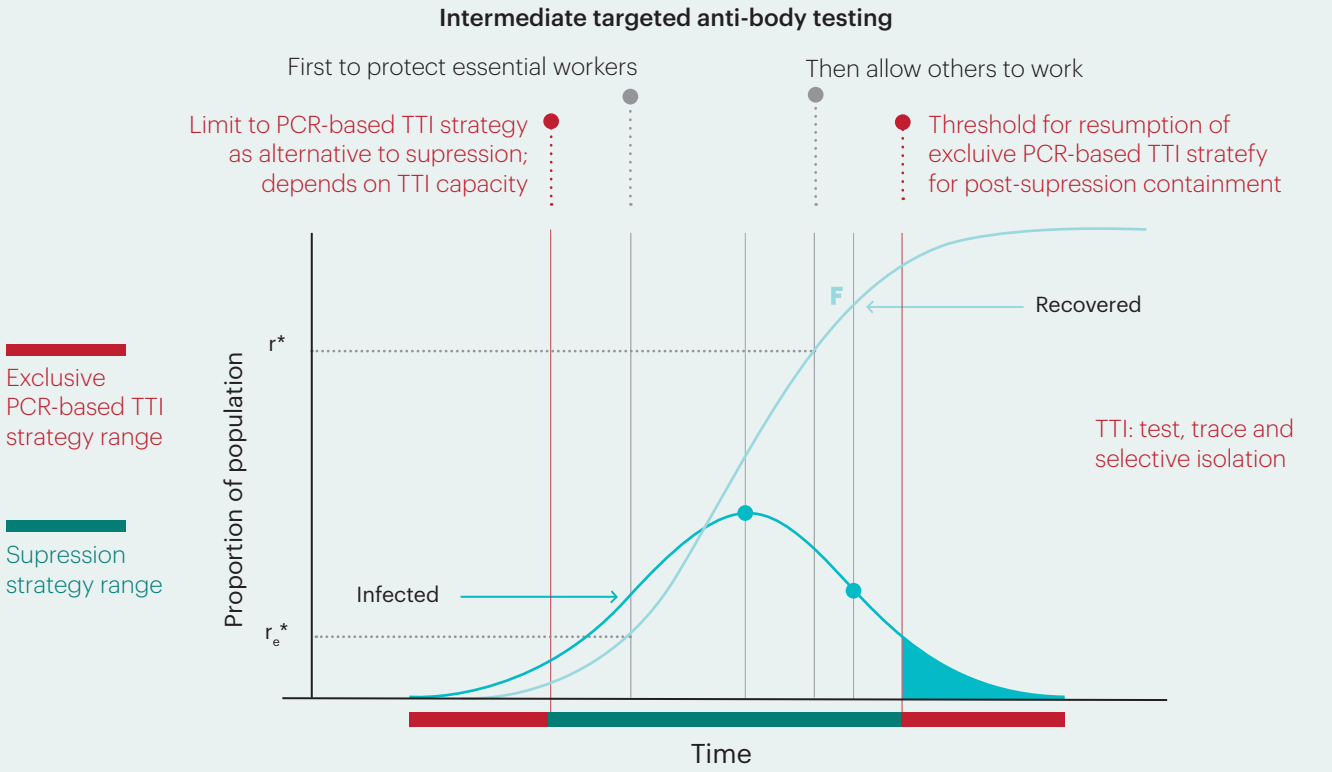
1. **Triaging symptomatic individuals in health care or community settings:** Highly sensitive rapid antibody tests are useful in settings with limited or no access to molecular tests. Provided resources are available, rapid tests can be used to test many symptomatic patients in the community or primary care level. Patients can then be quarantined to contain disease spread. This also provides quick testing results and reduces the load on molecular test infrastructures that are based in higher-level facilities. However, Africa CDC cautions that "negative antibody test in individuals with signs and symptoms suggestive of Covid-19 **does not** exclude the disease and a swab should be taken for molecular testing."

2. **Testing of contacts of confirmed Covid-19 cases:** Rapid tests are also a quicker and potentially cheaper means of testing all close contacts of a confirmed case. This is critical in interrupting the chain of transmission in the community. However, unless asymptomatic contacts are being tested daily, they should also be following quarantine protocols as recommended for those who are symptomatic or tested positive. Given the prudence in quarantining of all close contacts of a confirmed case, this strategy may not be an efficient use of resources.

3. **Informing situation analysis and serosurveillance:** Positive samples from any type of test done at surveillance sentinel sites can indicate Covid-19 transmission in the community.

World Bank. A World Bank analysis posits that the choice and mix of tests be selected with the aim of addressing the economic impact of the pandemic. In containment (pre- or post-suppression) stages of the disease, an exclusive PCR-based strategy for testing, tracing, and isolating those infected would be appropriate, while the remainder of the population return to work. However, this approach will be limited by the number of PCR-based tests that can be conducted within the country. If capacity for PCR is very limited or infections are rising (figure 3), antigen and antibody tests need to be leveraged to determine options for opening the economy.

Figure 3. Testing strategies based on number of infections



Note: The shape of the curve and the placement of the lines are stylized. Further, the figure does not show either the susceptible proportion of the population or the levels of infection that would have prevailed in the absence of any containment strategy. *F* depicts the proportion of the recovered population. r* = the recovered population proportion for which the benefits of a population-wide antibody test would just equal the costs of a population-wide antibody test; r_e* = lower threshold for proportion of subgroups, such as health workers; PCR = polymerase chain reaction;TTI = test, trace, and isolate.

Source: de Walque D, Friedman J, Gatti R, Mattoo A. How two tests can help contain Covid-19 and revive the economy. Research and policy briefs no. 29. World Bank.

At the time of the analysis, the World Bank researchers focused on antibody tests and their ability to confer immunity to individuals who were previously infected. Given the new evidence on potential temporary immunity to the coronavirus, however, antibody testing may not be cost-effective. Since the publication of this research from the World Bank, several Ag tests have come into the market that detect active infection from 1 to 14 days post-infection. However, while they may not be as sensitive as molecular tests, they could serve as a rapid means of triaging suspected cases and/or screening contacts exposed to infected individuals in settings where access to molecular testing is limited.

3. Selection of Tests

3.1 Evidence Based Selection Criteria

The routine policy process for introduction of new diagnostics in LMICs should involve stakeholder engagement with policy makers, disease programs, and laboratory network leadership. This usually leads to creation of a technical working group, which deliberates on the need, appropriateness, cost-effectiveness, budget impact, and feasibility of introduction. The technical working group would require the time to create national guidelines and operational plans for implementation. However, given the urgency surrounding the pandemic, standard deliberative processes may not be feasible.

Health Technology Assessment Framework

Since the 1970s, many countries (mostly high-income) have introduced the health technology assessment (HTA) as a systematic process for selection of health technologies to be introduced in their health systems. HTA is defined as "a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an efficient, equitable and high-quality health system." HTA principles and methods could be used to inform decisions regarding Covid-19 pandemic response.

It is true that HTA processes can involve a significant time investment for systematically assessing a new technology. Local governments and development partners could, however, leverage from the growing number of reports in the international literature to expedite development of a more systematic and evidence-based framework for selection of laboratory and diagnostic technologies for Covid-19. After expert review, major prioritization criteria can be adapted within the EOC and laboratory services response team for the pandemic. Appropriate criteria could include the following:

- Technical performance: specificity/sensitivity/time to result/sample type/reagents; stringent regulatory approval required
- Cost of technology (price and budget impact)
- Substantial variations in practice (may help bring efficiency compared to existing multiple testing platforms)
- Adverse event reports (or lack thereof)
- Potential impact on practice (significant change in protocols/training required/point of care)
- Potential impact on patient outcomes or management
- The need to make a health program acquisition or implementation decision (potential reasons: have donated products or a significant need to expand current limited testing capacity)
- Recent or anticipated "breakthrough" scientific findings
- Feasibility given resource constraints (funding, time, etc.)
- Public or political demand
- Scientific controversy or great interest among health professionals

In recent times, HTA processes have introduced "rapid reviews" in response to policy makers' requests for high-quality evidence on technologies in a short time frame. Rapid reviews have become an option for providing contextualized summaries of existing evidence in compressed time frames. In pressing times, policy makers do not have the option of conducting systematic reviews. The rapid review approach can

be adopted by the lab response teams for the pandemic to support selection of tests and provide updates with emerging evidence. Various repositories of evidence-based assessments have emerged recently, including those compiled by the Health Technology Assessment International (available at: https://htai.org/hta-support-for-Covid-19/online-resources/), among other global networks and think tanks.

ASSURED Framework

Médecins Sans Frontières developed the WHO-endorsed ASSURED (Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment-free and Deliverable to end-users) criteria that provides another technology selection framework, as presented in Table 2.

Table 2. ASSURED Framework–

Steps in selecting a diagnostic test	
Step 1: Define the test's purpose—why, what, where, who? • Decide whether an acute or chronic infection is to be diagnosed. • Decide whether the test is to be used for diagnosis, disease monitoring, or verifying a cure. • Decide whether the test should be quantitative or qualitative. • Decide whether test results will be analyzed at the point of care or in a central laboratory. • Define the test's end users: trained laboratory technicians or primary health care workers? • What is the required performance of the test?	**Step 2: Review the market** • Identify the products of interest available. • Obtain details of the tests available, including: (1) the manufacturer's name; (2) the product's name; (3) the product's catalog number; (4) package size; (5) storage requirements; (6) shelf life; (7) sample type (e.g., serum, plasma, whole blood, or urine) and volume required; (8) control reagents available; (9) instruction languages; (10) how long the test takes and the number of steps required; (11) additional equipment required; and (12) cost. • Determine whether analyzers are used and, if so, what the manufacturer's requirements are • for training, installation, and maintenance.
Step 3: Review regulatory approval by international and national bodies • Determine whether the test has the European conformity (CE) mark. • Determine whether the test has been approved by the US Food and Drug Administration (FDA). • Determine whether the test's manufacturing site meets the ISO 13485 standard. • Determine whether the test is prequalified or endorsed by WHO. • If not prequalified or endorsed by WHO, determine whether the test has been approved • by the Expert Review Panel of the Global Fund to Fight AIDS, Tuberculosis, and Malaria. • Determine whether the test has been approved by national authorities.	**Step 4: Determine the test's optimal diagnostic accuracy** • Review publications on the test's performance under ideal conditions (i.e., at reference laboratories). **Step 5: Determine the test's diagnostic accuracy in practice** • Review publications on the test's performance under real-life conditions (i.e., at the end-user level). **Step 6: Monitor the test in routine use** • Carry out quality control. • Carry out proficiency testing. • Supervise and train end users.

Source: Kosack C., Page AL., Klatser P. A guide to aid the selection of diagnostic tests. WHO 2017

A rapid review format can be adopted using the steps of the ASSURED framework to provide evidence to policy makers and support test selection.

3.2 Practical Trade-offs

As previously mentioned, the selection and use of tests will depend on the testing strategies being adopted by the country. WHO and other guiding bodies such as the Africa CDC have provided their own guidance on the types of tests and appropriate-use cases. Nevertheless, all countries face challenges in scaling up testing due to the finite quantity of supplies for tests and testing capacities. These are tough choices that countries are facing, particularly less affluent ones. Therefore, many countries will be required to keep the balance between full adherence to the recommended guidelines from national and international guiding bodies and using the evidence-based methods described above, while still pursuing prompt and sustainable action in the context of their limited available resources and time constraints.

4. Regulatory Strategy

Improving the availability of quality-assured diagnostic tests for infectious diseases remains a global priority. Unavailability of diagnostics, high costs of diagnostics, shortage of skilled personnel, and uncoordinated regulatory activities in LMICs deny individuals and health systems requiring lifesaving diagnostic services and treatments. Where diagnostic services exist, they are often under resourced, and amenities such as electricity and water may be unpredictable. Although national regulatory authorities (NRAs), and other institutions mandated to ensure the safety of populations, require that therapeutic, diagnostic, and medical device manufacturers obtain approval before use of their products on their country markets, the procedures for registration and regulation of these tools are frequently underdeveloped, complicated, and expensive, leading to market entry delays.

In LMICs, surges in Covid-19 positivity rates have led to an increased demand for diagnostics. At the same time, NRA capacity in LMICs vary considerably. For many LMICs, the Covid-19 pandemic has exacerbated existing regulatory challenges. Many LMICs with systematic regulatory gaps are becoming increasingly vulnerable as diagnostics of spurious quality enter their health care markets. This threat has compounded the negative effect weak local laboratory quality assurance capacity and slow responsiveness of their NRAs. The NRA global scoring system, the global benchmarking tool (GBT), provides the primary means by which WHO objectively evaluates the strength and identifies areas for improving drugs and vaccines' regulatory systems. However, the GBT does not assess the capacity of NRAs to regulate devices and diagnostics. Work is currently underway to integrate medical devices and in vitro diagnostics (IVDs) into the GBT.

According to WHO surveys, in 2018 only 30% of NRAs could effectively regulate medical products, although there was a higher capacity to regulate medicines and vaccines than other products, such as diagnostics. One way to combat the gap in capacity is through collaboration with different regulatory institutions. Many networks, such as the International Medical Devices Forum (IDMF) and the African Medical Devices Forum (AMDF), have been created to strengthen NRA regulatory functions in LMICs. The ADMF consists of experts from NRAs, laboratories, research institutions, African Society for Laboratory Medicines, Africa CDC, and WHO. For instance, the ADMF, through its working groups, has created a task force that focuses on addressing regulatory challenges related to Covid-19 in Africa. The four working groups of the Covid-19 Task Force have focused on:

1. Preparing a list of assessed commercial Covid-19 IVDs, using various regulatory approaches to confirm acceptable quality, safety, and performance
2. Updating a list of selected medical devices and protective, preventive equipment used in Covid-19 management
3. Proposing mechanism(s) to receive information on substandard and falsified diagnostic tests and other medical devices and disseminate such information to regulators on the continent
4. Developing a guidance document on the management of IVDs and medical devices donations for Covid-19

In an effort to facilitate access and mitigate supply chain interruptions, regulatory agencies have started adapting portions of their guidelines to enable deployment of Covid-19 diagnostics. Several NRAs have established assessment procedures to enable fast-track listing for authorization of Covid-19 IVDs. Approvals granted by regulatory entities such as the US FDA, the European Medicines Agency (EMA), and other stringent regulatory bodies are seen as quality and efficacy indicators. The United States expedited the availability of newly manufactured Covid-19 diagnostics by issuing emergency use authorization (EUA) guidance to manufacturers. In addition, WHO updated its Emergency Use Listing, or EUL, to evaluate IVDs in development. Essentially, EUAs and EULs facilitate market access and entry of novel diagnostics. Unsurprisingly, due to pressure for Covid-19 pandemic diagnostics, many rapid antibody–based assays are being sold and distributed without any independent assessment or validation. While the private sector has rallied to develop new diagnostics, efforts are needed to facilitate the channeling of these innovations into countries by promoting international collaboration and coordination, addressing regulatory the issues that can impede access for LMICs at a time where high demand and panic have caused shortages and barriers for the sharing of tests and technology. To assist LMICs' NRAs and decision makers in identifying and procuring quality diagnostics, the companion **diagnostic dashboard** provides an overview of the available diagnostic platforms and Covid-19 tests. The tool will allow countries to search for relevant tests on the market by using multiple parameters, including test type, sensitivity, and specificity, type of technology, regulatory status, and country of origin.

4.1 Strategies and Key Regulatory Considerations

Adapting Current Regulations in LMICs

In the short term, some countries should develop and adopt fast-track mechanisms for registering diagnostics, to reduce length of approval time and minimize confusion. In the long term, the national laboratory policies, guidelines legislation, and regulation may require reviews to enable diagnostics registration, including finalizing procedures for obtaining fast-track approval. Therefore, country-level Covid-19 EOCs and their management committees should, as part of their mandate, initiate discussions to review regulatory guidelines that will facilitate the import and use of much-needed Covid-19 diagnostics, kits, swabs, and reagents. Regulatory establishments should assess the potential risk for supply chain disruption for much-needed diagnostics based on their country's Covid-19 transmission and rate of spread of the SARS-CoV-2 virus. Countries should consider undertaking vulnerability risk assessments that mimic supply chain situations to enable appropriate interventions to address shortages in the medium-to-long term.

Management of Donations

There are limited policy guides that address the unique challenges that donations of diagnostics pose. The AMDF has guidelines for donations of IVDs. The AMDF guides the NRAs on how to swiftly authenticate quality, safety, and performance features of donated medical devices, including in vitro diagnostics during Covid-19. The AMDF recommends that all donations of devices and diagnostics must:

- Have the appropriate user manuals with detailed information on handling, installation, operation, maintenance, troubleshooting, precautions, and other relevant information.
- Depending on its nature and type, the donated medical device's labeling should have the following minimum information:
  1. The name of the medical device
  2. Model number or serial number
  3. Manufacturing and expiry date (where applicable)
  4. Life span or expectancy
  5. Name and address of the manufacturer
  6. Handling and storage requirement (s)

Moreover, the performance of IVDs must undergo verification studies at the national reference laboratory based on international standards including appropriate Clinical Laboratory Standard International (CLSI) standard(s), use of proper local clinical samples, and reference method(s).

5. Demand and Supply Planning

The Covid-19 pandemic poses significant supply chain challenges for LMICs. Ensuring that diagnostics are available is a key strategic component of global efforts to mitigate the impact of Covid-19. The quantification and procurement of Covid-19 tests, swabs, reagents, viral transport kits, and medium tests will depend on the testing strategy adopted by the country (see section on testing strategy). Accurate demand planning is essential to help countries justify and secure adequate funding to procure much-needed Covid-19 diagnostics. WHO's Covid-19 operational planning guidelines previously highlighted are listed again to reiterate steps needed to improve demand planning (table 3).

Table 3. Actions needed to build health system capacity for Covid-19 supply and demand

Step	Actions to be taken
1	Map available resources and supply systems in health and other sectors; conduct in-country inventory review of supplies based on WHO's: a) disease commodity package (DCP), b) Covid-19 patient kit, and c) Covid-19 Supply Chain System (CSCS). Identify central stock reserves, if available, for Covid-19 case management.
2	Implement supply chain control and management system (stockpiling, storage, security, transportation, and distribution arrangements) for medical and other essential supplies, including Covid-19 DCP and patient kit reserve. Review procurement processes (including importation and customs) for medical and other essential supplies, and encourage local sourcing of high-quality products to increase timely access to supplies. Assess the capacity of the local market to meet the increased demand for medical and other essential supplies, and coordinate requests for critical items to the CSCS through the Covid-19 Supply Portal on the Covid-19 Partners Platform. Conduct regular review of supplies; develop a central stock reserve for testing and case management of Covid-19. Prepare staff surge capacity and deployment mechanisms; health advisories (guidelines and standard operating procedures); predeployment and postdeployment packages (briefings, recommended/mandatory vaccinations, enhanced medical travel kits, psychosocial and psychological support including peer support groups) to ensure staff well-being.
3	Identify and support critical functions that must continue during a widespread outbreak of Covid-19, such as water and sanitation, fuel and energy, food; telecommunications/ Internet, finance, law and order, education, transportation, and essential workforce.

Source: WHO's Operational Planning Guidelines to Support Country Preparedness and Response

In line with WHO's recommendations on pandemic logistics and operational planning, an initial step for effective diagnostic demand planning is to conduct a rapid review of the in-country inventory of accredited laboratories, qualified laboratory personnel, and diagnostics machines/platforms at the national, regional, and community levels, including in the private sector. This enables LMICs to determine their existing Covid-19 testing capacity. Since existing diagnostic testing capacity could either be

overstretched or underused, LMICs need to match the supply and demand of required diagnostics with the existing test management capacity. National epidemic management committees need to maintain testing capacity visibility and establish procedures to maximize the current laboratory capacity in the short term to minimize supply chain bottlenecks. A transparently maintained test absorption capacity reduces the risk of waste due to overestimating diagnostics, related reagents, test cartridges, swabs, and transportation kits.

5.1 Supply Bottlenecks for Covid-19 diagnostics

Visibility Across the Supply Chain: A diagnostics supply chain typically consists of four levels, integrated to accomplish efficient flow and achieve optimal cost: (1) raw material supply, (2) manufacture, (3) delivery of products (logistics), and (4) offer of testing services. In the particular case of Covid-19 response, these four levels will require further consideration, as discussed below.

Raw material supply. Typically, raw material suppliers and manufacturers have built-in agreements to ensure that shipments move along the chain at specific times. However, even under ordinary circumstances, this often does not happen as efficiently as planned. The additional pressure caused by Covid-19 has led to closures and slowdowns at raw material factories. The overdependence on a limited number of manufacturers created significant risks, limiting the number of diagnostic suppliers. Additionally, grounded flights and travel restrictions issued by countries resulted in failed supplies, unanticipated delays of raw materials to manufacturing sites, and made estimated-time-of-arrival (ETA) calculations for raw materials and goods unreliable. Inconsistent ETAs create multiple negative effects for manufacturers and for the distribution of diagnostics. Beyond the bottleneck of materials and goods, the prices of raw materials, cost of transporting raw materials, and cost of finished diagnostics also increased four- to fivefold in many instances.

Manufacturing. Manufacturing operations have been disrupted due to Covid-19. Many countries were unprepared for plant closures, and their lack of production scheduling agility was made evident by the pandemic. The global capacity to meet the scale of the challenge was insufficient during the early days of the pandemic. Initial production was carried out to meet shortages locally, where relevant industries were based, rather than globally. Much of the equipment emerging from the initial constrained manufacturing was costly, especially when local economies had been hit due to lockdown measures. Countries such as England, China, and the United States required nontraditional manufacturers to convert parts of their production lines to making COVID diagnostics, kits, and personal protective equipment (PPE). Clearly, product innovation and novel manufacturing pipelines are required. High demand for traditionally manufactured devices, challenged by global demand and limited production, also resulted in a call for additive manufactured (3D-printed) equipment to fill the gap between traditional manufacturing cycles. The easing of lockdown measures, leading to reopening of fabrication facilities, has led to the production of a number of new rapid immunochromatographic; in addition, ELISA immunoassay tests have been developed and produced by different manufacturers for the diagnosis of s.

Delivery of products (logistics). As the Covid-19 pandemic continues to spread, it has exposed vulnerabilities of supply chains and logistics. It has disrupted health supply chains, affecting active pharmaceutical ingredients, shipping, procurements, finished health care products and more. Health care logistics supply chain entails much more than the movement of health care products, and other related products, between markets. It definitely deals with problems at the grassroots level, including

the availability of labor in industrial units, transportation activities, especially transporters and couriers and how they function in a timely manner. All these factors cause delays and hamper the supply chain, causing issues in supplies of diagnostics, medical equipment, raw material, and much more. Supply chain bottlenecks occur when there is lack of visibility or inability to track shipments, and these are worsened during a pandemic. To maintain the supply chain for diagnostics and reagents for Covid-19, global, national, and laboratory systems must prioritize resilience and visibility along the chain. Countries should leverage the revolution in information technology to increase the uptake of diagnostics in health care and during epidemics.

Offer of testing services: In many LMICs, delivery of health service provision is through the public and private sector. The private sector is usually made up of a combination of for-profit and non-for-profit health services. Effective mobilization of the non-for-profit sector, comprised predominantly of faith-based health facilities, will enhance access to point of care (POC) and near-POC testing in communities. Overall, logistics entities play a critical role at all points in the testing supply chain. The shipment of components from sources around the world to testing laboratories and the transportation of samples from collection points to laboratories are especially critical to support testing in LMICs.

Proprietary Equipment: The dependence of public and private labs on automated testing and use of closed-system equipment increased the supply chain challenges and reduced availability of much needed tests. Closed systems require health systems to use proprietary chemical kits made by a small number of manufacturers, which causes a key bottleneck even if the equipment has capacity to conduct many more tests. A key reason that laboratories with closed-system equipment have been underused during the current pandemic is a shortage of the cartridges loaded with proprietary reagents. To exploit these systems nearer to their theoretical maximum capacities, brand equipment manufacturers will need to increase production volume, yet doing so has remained a tough decision to make, given the costs involved and the risks when long-term demand appeared uncertain during the onset of the pandemic. Global suppliers will now have to consider adequate contingency: surplus inventory supply, inventory safety stock, higher sales-to-inventory ratios with multiple suppliers, and having suppliers closer to consumption markets to protect and offer business continuity during the next pandemic. There is also a need to scale up production of closed system cartridges and proprietary reagents. Global effort and regional efforts such as ACT, PAN, and PACT in Africa have helped streamline supply chains and advocate for additional production from manufacturers. However, LMICs will need to continue to monitor the pipeline of new technologies for early access. The companion dashboard to this document provides a regularly updated list of quality assured tests available that countries can use to monitor the pipeline.

5.2 Considerations for Quantification of Covid-19 Diagnostics and Tests

Quantification consists of estimating quantities and costs of products required for a specific health program (or service), and determining when orders should be placed and delivered; it provides estimates of what needs to be procured and when. A quantification exercise's result informs high-level decision making on financing and procurement of health products, as well as estimation of storage and transportation needs. It is a continuous process that requires regular monitoring and updates, and relies on a functioning supply chain system. Quantification has two major components: namely forecasting and supply planning. ***Forecasting*** is the process of estimating the quantities and costs of products required to meet customer demand during a particular time frame in the future. At the same time, ***supply planning*** is the process of estimating quantities and total costs of products required for procurement and

determining order quantities and desired receipt dates of shipments. Effective and efficient quantification exercises help public health interventions ensure optimal availability of the right health products, including diagnostics, and reduce wastages.

The processes, principles, and methodologies used for estimating Covid-19 laboratory diagnostic requirements are similar to that of commodities for other diseases. Countries, particularly LMICs, can use the experiences and expertise garnered by managing other health programs such as HIV and AIDS, malaria, and TB to estimate Covid-19 diagnostics requirements.

A functional and well-represented quantification technical working group/committee, which is usually a subgroup under a more comprehensive supply chain working group, is established to lead and coordinate quantification activities. Such a coordination mechanism strengthens the supply chain for COVID diagnostics and facilitates coordination, information sharing, and timely decision making, increases commitment from government and donors, and promotes the credibility of processes and results. The following steps may be taken to set up and capacitate the coordination mechanisms for the diagnostic quantification:

1. Assess stakeholders and decision makers needed for the laboratory and diagnostics supply chain.
2. Outline the roles of the stakeholders and decision makers in the supply chain.
3. Select and notify the major stakeholders to be part of national quantification committee (epidemiologists, national reference laboratories, laboratory experts, regulatory authority, donors, health facilities, central medical stores and storage facilities, implementing partners, academics, and societies).
4. Establish the quantification committee with agreed-upon and approved terms of reference and standard operating procedures for the committee to define the roles and activities of the members.
5. Provide orientation and training on role expectation as necessary.

Note: In Ethiopia, the Philippines and Ghana, multidisciplinary advisory committees with members from professional associations and volunteer experts have been created, contributing to a rapid, comprehensive, and successful response to emergency needs.

Roles and responsibilities of the quantification working group/committee should include:

- Defining the quantification scope in terms of the type of diagnostic machines, variety of tests and test platforms, reagents, and supplies; geographic/sector coverage of the quantification (e.g., central level vs. regional/district or public vs. private); period of quantification, etc. The quantification needs to reflect the Covid-19 testing strategy for the country.
- Defining the processes, methodologies, and tools for the quantification exercise
- Defining, collecting, and analyzing data for the quantification. The preparation of a checklist for data collection is helpful. See section immediately below for the comprehensive list of data required for quantification of Covid-19 diagnostic commodities and other considerations.
- Developing draft assumptions and results. Quantification technical working groups should develop assumptions based on available evidence, including expert opinion, when data are not available. Using the draft assumptions and the selected tool(s), the team should develop draft quantification results: estimated demand, quantity to order, total cost of procurement, and timelines for ordering and receiving.

- Coordinating and facilitating quantification exercises with all pertinent stakeholders' involvement to validate and agree on the assumptions and results of the quantification: development of short-, medium- and long-term procurement estimations of Covid-19 diagnostics to inform procurement and resource mobilization. Several countries have conducted successful quantification validation workshops, and other supply chain discussions, using electronic media such as Zoom, Google Meet, or Skype. during the pandemic; examples include Ethiopia, Madagascar, and the Philippines.
- Documenting and disseminating quantification processes, methodologies, assumptions, results and challenges, obtaining the necessary approvals from decision makers, and following up on procurement and delivery processes
- Regularly monitoring data on testing capacity (number of testing machines, laboratory staff, training, approvals of laboratories), number of tests performed, seropositivity rates, actual consumption of commodities, usage rates per test, stock on hand, expiry dates, stock on order, stock status, et cetera
- Regularly revising quantifications as up-to-date data become available to make necessary adjustments on procurement requirements, orders, and resource requirements

5.3 Data for Quantification

The novel coronavirus is new, but knowledge about Covid-19 and pandemic control measures is growing every day. Therefore, assumptions must be evidence-based as much as possible. Figure 4 presents a list of data/evidence required for initial and or subsequent quantification exercises.

Figure 4. Data needs for quantification

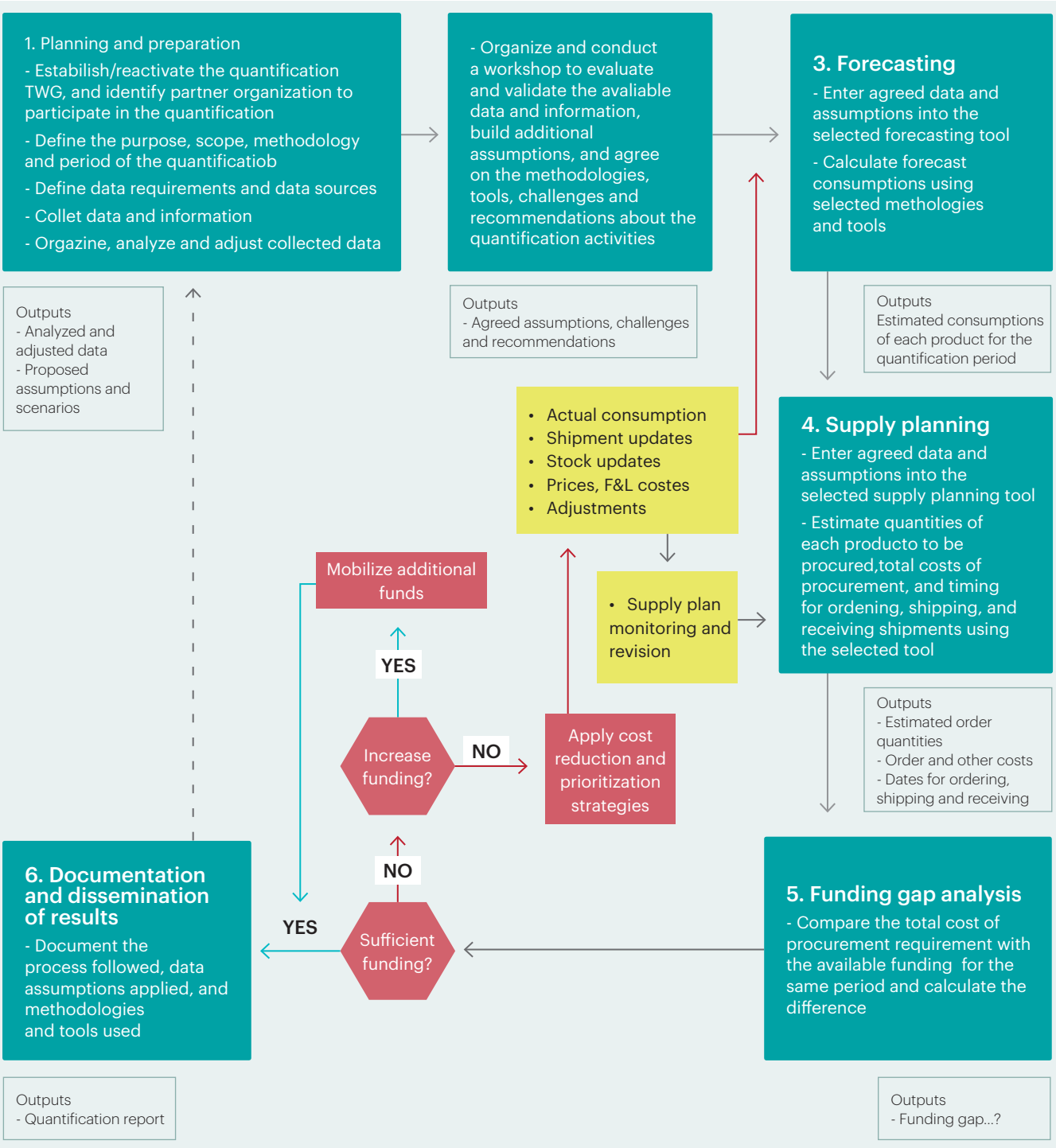
Data needs for quantification of Covid-19 testing reagents and supplies using capacity-based morbidity method

- Incidence rates and the total number of estimated Covid-19 infections in the country/ region considered during a defined period disaggregated by clinical stages
- The target number of Covid-19 tests estimated to be conducted based on existing testing capacity, testing strategies, the proportion of repeat screening tests, and quality control and training requirements...
- The testing strategy adopted by the Covid-19 Emergency management team and public health officials
- List of functioning Covid-19 testing platforms/ machines and respective reagents and supplies
- Testing throughput of each Covid-19 testing platform per day
- The proportion of estimated Covid-19 tests conducted using each platform (if more than one platform is available)
- Usage rate of each reagent and supply per test by type
- Wastage rates
- Buffer, minimum and maximum stock level policies
- Stock of tests on hand and corresponding expiry dates (from all levels if possible)
- Stock on order
- Unit prices of each reagent and supply
- Freight and other logistics costs
- Available funding including in-kind and cash donations
- Lead times
- Shipment intervals
- The actual number of tests conducted.
- Actual consumption of each commodity

Source: Developed by Authors

When local data are not available, as in the case of this epidemic for many countries, the teams shall consider experience and research findings from other countries and expert opinion; however, systems must be set up for collection and analysis of required service and logistics data so that future decisions are based to a greater extent on the local context. Figure 5 provides an overview of the quantification process, which is described in detail in the remainder of this chapter.

Figure 5. Quantification process for commodities



Source: Developed by Authors

Estimation of the number of Covid-19 diagnostic tests for the quantification period: Several methods can be used to develop forecasts of demand for Covid-19 diagnostics. For a new and growing epidemic such as Covid-19, data on previous consumption will most likely not be available; thus, the morbidity method is appropriate for forecasting needs until more reliable consumption data are available and testing capacity is saturated. The Covid-19 positivity data from epidemiologists and rates of mild and severe infections are all beneficial inputs for quantification based on morbidity. On the other hand, estimating the number of samples to be tested during a pandemic is usually tricky. Several factors must be considered before the quantification team agrees on the estimated number of tests for the quantification period. These considerations should be made:

- Testing capacity in terms of the number of approved laboratories, trained laboratory personnel, number of testing machines and their throughputs, and potential testing capacity scale-ups/increases. Countries have increased their testing capacity after a quick assessment of available testing machines and refurbishing the nonfunctional platforms/machines. It is also vital to assess needs for increasing testing capacity and advise decision makers, especially if the existing testing and management capacity is markedly incommensurate to the expected number of COVID-cases.
- How best to estimate number of cases. Estimating the number of Covid-19 cases based on the most likely epidemiological estimation scenario, and including the proportion of cases by clinical stages (mild, moderate, severe, and critical), should be considered. This classification will better estimate cases to be tested, especially if testing strategies are segmented.
- Testing strategies. Depending on capacity, funding, and/or availability of test kits, LMICs may decide to test only most at-risk populations, people with signs and symptoms, or the whole population. The strategy will determine the number of tests to be conducted irrespective of the total Covid-19 cases as estimated based on epidemiological modeling. The selected strategy determines the positivity rates expected from testing.
- Protocols/policies/algorithms on the number of repeat and confirmatory tests. These will also affect the total number of tests to be conducted; the confirmed case will need to have repeat tests to confirm recovery from Covid-19, and this needs to be considered in estimating the total number of tests to be ordered per period.
- Additional demands for testing, such as training and quality control

List of products with full specification: The quantification team in consultation with other stakeholders (such as the regulatory authority, procurement units, and central reference laboratory) should decide on the type of and full specifications of Covid-19 diagnostic tests, reagents, and supplies. Each product's full specification has to be provided, including name description, storage conditions, and pack sizes. If multiple platforms are to be used for testing, different groups of testing reagents and supplies may need to be selected and quantified. Selecting reagents and supplies that can be used on multiple types of platforms is advised when possible to get economies of scale and reduce the need for carrying out multiple procurements, which would result in greater cost to the Covid-19 interventions. The selection should also consider the availability and ease of diagnostics from the market. The Rockefeller Foundation dashboard enables countries to identify approved products and their specifications.

Product and logistics costs: Due to high demand and logistics challenges caused by the Covid-19 pandemic, unit prices of testing reagents and supplies and freight and logistics costs have been reported to be relatively high; thus, quantification teams need to consider more realistic unit costs and include contingency when estimating funding requirements. The WHO and Foundation for Innovative New

Diagnostics (FIND) databases provide prices of some diagnostics tests, reagents, and supplies; users can click on the links to see details. There are procurement platforms at the African and South American continental level and at the global level for pooled procurements of Covid-19 diagnostics to help optimize prices during procurement.

Supply planning: It is crucial to make sure that supply planning is conducted in addition to forecasting (estimating demand for testing). This requires determining available stock on hand and corresponding expiry dates, stock on order and diagnostics promised in donations, wastage rates, and buffer stock levels. Lead times, shipment intervals, freight, and other logistics costs also need to be factored in to determine procurement requirements in terms of quantity, total cost, and timelines for ordering and receiving shipments.

Funding gap analysis: Quantification teams should conduct funding gap analysis (i.e., comparing the total cost of procurement against the available funding) during each quantification exercise to identify any additional need to mobilize resources for the future procurement needs. In-kind or cash donations from local and international donors should be considered when conducting such an analysis. If it is impossible to fill an identified funding gap, quantification technical working groups/committees need to revise the quantification to reduce the procurement requirement until the requirement can be filled with the available funding. Approaches for reducing requirements include reducing buffer levels, changing testing strategies to those that can yield the same number of Covid-19 cases with a smaller number of tests, and replacing expensive commodities with less costly alternatives.

Quantification tools: A primary forecasting tool such as the WHO Covid-19 Essential supplies Forecasting Tool (COVID-ESFT) can be used to forecast needs. This tool is not a complete quantification tool, and only provides estimated demand based on the capacity for testing and management of Covid-19; quantification technical working groups need to consider the supply planning parameters mentioned above (stock on hand, buffer levels, wastages, etc.) to estimate procurement requirements. In addition, the tool does not consider the requirements for training. The US Agency for International Development's Medicines, Technologies, and Pharmaceutical Services (MTaPS) program has developed an Excel®-based quantification tool that can support both forecasting and supply planning; it is being tested in Bangladesh and the Philippines and can be made available on request.

Documentation and dissemination: Once the quantification exercise for Covid-19 diagnostics is concluded, quantification working groups should document and disseminate processes followed, methodologies used, assumptions, results, and challenges. Its report should also indicate the stakeholders involved in the quantification and include proposed solutions to challenges encountered during the quantification exercises.

Revisions of quantifications: Due to the pandemic's rapidly changing nature, frequent reviews of quantifications are advised since it is difficult to predict disease progression and transmission patterns. It is important that quantification working groups meet regularly (at least monthly or quarterly), to update and revise the quantifications, making necessary adjustments as updated and more accurate data/information become available. Using multiple methodologies, both consumption and morbidity methods, and comparing results to identify areas that need further modifications are recommended as such data become available.

6. Procurement Considerations for Covid-19 diagnostics commodities

The Covid-19 pandemic has indeed placed heavy stresses on the existing procurement and supply systems for diagnostics globally. National-level procurement procedures in many LMICs involve developing a procurement plan, establishing contract terms with prospective suppliers, managing tenders, assuring the quality of products, and ensuring adherence to contract terms. However, because the pandemic is an emergency, fast and very pragmatic solutions need to be implemented in LMICs. Many countries have had to activate emergency procurement regulations and procedures, including registration and waivers for import of products from a regulatory authority. Since the diagnostic reagents and supplies, if not the platforms, may be new to many LMICs, it is unlikely that they are previously registered and approved for importation by the countries' NRAs. Countries need to introduce new and flexible regulations or override existing regulations to allow importations of such products quickly. One approach used by LMICs is to allow imports of products manufactured by WHO-recommended manufacturers/supplies.

6.1 Methods and Options for Procurement

Most effective methods for the emergency: Direct/sole sourcing and restricted bids need to be adopted to ensure faster delivery of Covid-19 diagnostics. Direct sourcing is also justified because of the limited number of suppliers for diagnostic products. Pricing interventions need to be considered to ensure efficiency in procurement.

Price Negotiation Options

- **Performance-based pricing:** Pay-for-performance or risk-sharing approaches have emerged in the last few years. These payment schemes are based on the performance of the product, which is tracked in a defined patient population. The payment for the product is based on the health and cost outcomes achieved in the real life use of a novel health product. A predetermined contract outlines payment conditions for various levels of performance anticipated. These types of pricing agreements have been useful for novel products, such as emerging Covid-19 diagnostics, which as yet do not have sufficient clinical and economic outcome data. One of the main determinants of a fair, value-based price for diagnostics is availability of data surrounding the benefits of the technology and the epidemiology, in this case, of Covid-19 itself. Several factors go into the pricing framework for diagnostics, but the overarching driver is the technologies' long-term benefits, which is used to determine the technologies' long-term value and lets payers or manufacturers undertake projections of a value-based price.
- **Differential pricing:** Many manufacturers of diagnostics practice third-party price discrimination as they routinely set different prices for different markets. Usually, the prices for LMICs are set at a lower rate compared to the developed world. Countries should explore if such opportunities exist for Covid-19 diagnostics in their market. Some diagnostic manufacturers also seek payments on a basis that takes account of the value that they add to the care pathway. However, a number of developers indicate that anticipated pricing is largely estimated according to cost-plus basis to ensure sufficient profit margin, rather than on a value-based approach.

Though Covid-19 is the first pandemic of this scale to occur in 100 years, the past decade has seen many epidemics (e.g., SARS, Avian influenza, and Ebola), which have resulted in fast-tracked diagnostics and EUA of various tests. There might be lessons to learn from those experiences for price negotiations. Additionally, the size of the population who will benefit from new technologies often plays some role in pricing, especially when considering the budget impact of the new technology. Finally, the willingness of society or payers to pay more during a pandemic may be greater than during ordinary, or noncritical times.

Procurement through International Procurement Agencies

If the local procurement capacity is weak or not functional, it may be worth considering international procurement agencies that may have the capacity for negotiations because of economy of scale and the ability to conduct faster procurement processes. When it comes to Covid-19 diagnostics for LMICs, there are a few important international initiatives focused on scaling up manufacturing, pooled procurement, and collaboration; these are outlined below.

United Nations Covid-19 Supply Chain Task Force

In early April 2020, the United Nations (UN) launched the UN Covid-19 Supply Chain Task Force—coordinated by WHO and the World Food Programme—to massively scale up the procurement and delivery of PPE, testing and diagnostics supplies, and biomedical equipment such as ventilators and oxygen concentrators. The task force leveraged each partner's capabilities and expertise into a mega-consortium to identify procurement needs and better negotiate with suppliers.

The task force ensures the establishment and function of the Emergency Global Supply Chain System through the following actions:

1. Obtain through WHO, a dynamic understanding of supplies required to halt Covid-19's spread. WHO has developed a catalog for a prioritized selection of items, including diagnostics, that can be ordered using this mechanism

   (https://www.who.int/docs/default-source/coronaviruse/20200417-catalogue-v1.pdf?sfvrsn=ddd851d5_6).

   The companion dashboard to this document, an additional resource for LMICs, provides an updated list of the most recently approved tests to aid countries.
2. Identify and map safe sources of lifesaving Covid-19 supplies:
   - The task force uses available public and private sourcing mechanisms to access existing global suppliers and identify potential new suppliers.
   - Task force members coordinate negotiations and procurement with key suppliers.
   - The task force agrees on allocation principles based on need, gap, and absorption capacity.
3. Deploy allocation (ordering and receiving) mechanisms:
   - Health agencies will need to be registered at the country level through the UN Resident Coordinator or Humanitarian Coordinator office to access the partner platform (https://Covid-19-response.org/) to upload information on their demand for critical items. The task force operates under the assumption that quantities of diagnostics being entered on the platform have the necessary financial commitments backing them.
   - Once country quantities are entered, the task force administrator will confirm the demand

priority, reject the request, or hold the request until further notice.
- The requests will be allocated to purchasing agencies centrally. Membership in each of the purchasing consortia (comprising PPE, diagnostics, and oxygen equipment) varies but includes, among others, WHO, the United Nations Children's Fund (UNICEF), the UN Development Programme, United Nations Office for Project Services, the Global Fund, the World Bank, Unitaid, the Pan-American Health Organization, Africa CDC, Bill & Melinda Gates Foundation, FIND, the Clinton Health Access Initiative, the UK Department for International Development, and PATH.
- By mid-August 2020, more than 125 countries were already using the platform, and more than 50 donors have recorded contributions on the platform.
- A complete guide on the ordering and receiving process is available from https://Covid-19-response.org/.

4. Establish global logistics distribution system:
   - The task force operates a hub-and-spoke distribution chain to optimize needs and supplies for each category of commodities (i.e., PPE, diagnostics, and oxygen and oxygen-based equipment).

ACT Accelerator Diagnostics Partnership

The co-conveners for this partnership are FIND and the Global Fund, partnerships with WHO, the World Bank, UNICEF, and Unitaid, the Bill & Melinda Gates, and the Wellcome Trust. It was launched on April 24, 2020, to accelerate the development, production, and equitable global access to new Covid-19 essential health technology. The activities of the ACT Accelerator align with that of the UN Covid-19 Supply Task Force.

6.2 Supplier Identification

1. **International procurement:** WHO and other organizations listed above have lists of identified reliable suppliers/manufacturers of Covid-19 diagnostics, as mentioned earlier. It is recommended that countries consult the relevant websites for updates.

2. **Local sources:** LMICs should assess local capacity for the production of diagnostics. Recent media reports have noted that countries like India, Bangladesh, and Senegal, are considering producing tests locally.

3. **Donations:** A number of counties have been able to receive donations from the developed world. It is essential to exert a comprehensive and coordinated effort to identify, approach, and make requests of potential donors as interim solutions to such products' global shortage.

6.3 Additional Procurement Considerations

Incoterms®: The Incoterms to be applied need to be specified in the tender procurement if the LMIC is sourcing directly from manufacturers rather than through large pooled procurement systems as described above. Incoterms and shipping documents need to be sent to suppliers, among other

considerations covered in this document, and may need to be negotiated after selection of the supplier. This has implications for the total cost of delivery. The Incoterm selection needs to consider total cost analysis, availability, cost, and efficiency of insurance and logistics companies to take care of the shipment from the country of manufacture up to delivery.

Shelf-life requirements: Despite the ravaging nature of the pandemic and the emergency mode of most procurements, countries need to specify the shelf-life requirements of diagnostics to be procured. Many drug regulatory authorities and institutions that purchase medical products have specific requirements for remaining shelf-lives of products at the time of delivery (ranging from 70% to 80% of the total shelf-lives). If the remaining shelf-lives of supplied products do not meet the requirements, the products can still be used before expiry specified.

Lead times: Covid-19 diagnostic platforms, testing reagents, and supplies are in unprecedented global demand, and this, coupled with the limited suppliers of such product, means that lead times for procurement are unpredictable. Better planning and early submission of orders can help ensure earlier delivery of products; to achieve this requires streamlined, coordinated, and fast decision making in supply chain management, including procurement. Related to this is the importance of procuring and delivering full test components, including supplies, at the same or very close delivery times. Missing components lead to increased expenses. The tender document needs to specify the date for delivery of all test-product components to make it valid and efficient.

Freight and logistics costs: Increased demand, low capacity, and emergency surcharges have increased freight and logistics costs. According to the *Journal of Commerce,* for example, "Between March and April 2020, the per kilo price of air freight from Shanghai to Frankfurt jumped nearly 300%, rising from $2.46 to $9.64." Countries need to consider this significant increase in freight and logistics costs when planning for and undertaking procurements. It might also be worth considering suppliers with which freight and logistics costs may be lower. Because of the immediate demand for emergency delivery, air shipments are preferred to the ocean; however, going forward and if the longer-term estimations can be done with better availability of data, shifting to ocean shipments save a significant amount of money that can, in turn, be invested in procurement of more diagnostic products.

Prepayments: Some suppliers may require prepayment, and the procurement organizations need to have flexible procurement regulations to allow this; otherwise, they need to negotiate effectively with the suppliers to avoid prepayment. However, prepayments may have advantages, such as discounts from suppliers.

Procurement contract performance monitoring systems: LMICs need to establish and implement a system to monitor the contract performance of suppliers, the products procured, and the procurement agent, and take appropriate actions based on the results. Parameters that need to be measured and monitored include:

- Delivery timelines
- Adherence to technical, packaging, and labeling specifications
- Shelf life requirements
- Other terms and conditions
- Quality, safety, and efficacy of products
- On time payment

7. Considerations for Distribution and Warehousing of Covid-19 Diagnostics

The principal goal for distribution in LMICs during the Covid-19 pandemic is to ensure a steady supply of diagnostic tests, reagents, swabs, and kits. LMICs must also ensure the efficient use of limited resources. Distribution costs, including storage and transportation, can be substantial components of the Covid-19 diagnostic supply chain. Therefore, planning/designing a new system or repurposing an existing one for distributing diagnostics during the pandemic could be complicated, with significant in-country effects. For the already-stretched logistics and distribution systems in LMICs, the pandemic will present unexpected challenges requiring a reconsideration of ways to optimize existing logistic infrastructure within countries. Effective diagnostics, reagent, and swab distribution systems rely on sound system design and the right management approach. The Covid-19 context and testing strategy in LMICs will largely influence the test distribution system's design. A well-designed and well-managed distribution system should:

- Maintain a constant supply of tests, and accompanying reagents
- Keep tests, reagents, and associated testing materials in the right conditions throughout the distribution process
- Minimize Covid-19 diagnostics losses caused by spoilage, poor storage, and expiry
- Maintain accurate inventory records
- Optimize storage points/location
- Support near-POC testing arrangements, especially for centralized test sites
- Utilize both public and third-party private logistics systems to ensure efficiencies and effectiveness in distribution, storage, and transport
- Reduce misappropriation of lab resources, theft, and diversions
- Provide information for forecasting demands on an ongoing basis

7.1 Managing Distribution

The Covid-19 diagnostics distribution and warehousing processes start when manufacturers or suppliers dispatch tests to countries. The distribution and warehousing cycle restarts when labs conduct tests, and information on quantities consumed are reported to the procurement group or unit. The distribution strategy could be changed as the transmission dynamics change as the pandemic evolves.

In LMICs, the following steps are worth managing effectively to ensure the steady flow of tests during the pandemic:

- Port clearing (for imported diagnostics). Shipment documents, including air waybills, bill of lading, and certificate of analysis, will have to be sent by suppliers before the arrival of Covid-19 diagnostics to enable preshipment port-clearing activities, including obtaining tax and import duty waivers, as well as approval from the NRA if required.
- Receipt and inspection of diagnostics
- Transport from port
- Inventory and storage
- A "push" model of test supply to labs in the short term. In the medium-to-long term, requisition based on consumption could be made to test sites.

- Conducting tests at both central and peripheral sites
- Reporting of consumption

The required distribution and warehousing parameters for LMICs to consider during the Covid-19 pandemic include testing strategy, degree of centralization of tests, number of levels or sites of tests, geographic distribution of test sites, health facility–based or national laboratory–based test sites and the population coverage.

Many LMICs will rely on or modify the existing logistics infrastructure and/or design a new system. An approach that changes the existing systems to introduce an informed push system while consolidating storage points, introducing transport loops, and increasing human resource capacity for distribution is recommended. Whichever distribution approach is adopted, it will be served well if a rapid option or cost analysis is done to support decision making to assure the availability of appropriate storage, transport, and above all, the required human resources for effective and improved access to tests by all.

Once diagnostics tests arrive and are inventoried, the local storage processes should align with the manufacturer's specifications. The potency of some health products and test kits depends on the temperature of storage. Some tests and reagents may require refrigeration and storage below the ambient temperature, while others can be stored at room temperature. If no specific storage directives are given, normal storage conditions apply: store in dry, well-ventilated premises at temperatures of 15°C–25°C or, depending on climatic conditions, up to 30°C. It is important to check storage temperatures in each storage zone regularly.

7.2 Sample Transport Protocols

The packing and delivery of clinical specimens to the laboratory should be as quick as possible after collection. Proper management of samples during transportation is essential. Specimens that can be delivered promptly to the laboratory can be stored and shipped at 2°C–8°C. When a delay is likely in specimens reaching the laboratory, the viral transport medium's use is strongly recommended. National regulations and protocols for transporting specimens within LMICs should be developed. The lab team should label samples correctly. The distribution team should design a system to alert the laboratory before sending specimens. This will boost the proper and timely handling of samples and timely reporting.

8. Financing and Budgeting Considerations

The Covid-19 pandemic has highlighted the need for investment in health systems to tackle public health emergencies. Therefore, policy measures need to be designed to address the long-term goal of health systems strengthening. WHO recommends taking the perspective of investing in "common goods for health," which include robust surveillance systems (including laboratories), data and information systems, regulations, and communication and information campaigns. Additionally, all financial barriers to health care access need to be removed, including fees (e.g., for testing), copayments, and lack of social support to ease access (e.g., free transport or replacement of lost income). Immediate actions need to be based on a foundation of increased prioritization of health by the government and sustainable policies that will build resilient health systems.

WHO and the International Monetary Fund recommend immediate action be taken to increase resources allocated to the health sector in response to the pandemic. However, these changes need to be made carefully, keeping in mind the stage of the outbreak and country-specific factors such as demography, health system capacity and infrastructure, costs of resources, et cetera. Important actions recommended include:

1. Reprogram government funds and initiate use of emergency funds (if available) for the health sector for immediate needs.
2. Create a specific program for Covid-19; depending on the country, this may require special legislation to create the program. The program should be comprehensive and include budget for laboratory needs and associate supply chain costs.
3. Expedite fund transfers to subnational agencies, governments, health service providers, and other service/goods providers for the response. Ensure that payment is timely for vendors and providers for the smooth functioning of the response. Advance payments could be another option (if feasible) to secure access to resources, especially diagnostics that are in high demand.
4. Provide flexibility in the use of funding and simplification of procurement processes. However, a balance between control measures and flexibility is important. Risk-based control measures could be a useful strategy where high-cost transactions such as purchase of equipment or infrastructure could face greater scrutiny.
5. Pair all of the above measures with adequate monitoring and evidence collection, comprising these steps:

    a. Gather information on what is working and what is not to ensure quick course correction. There is increasing evidence on the impact of nonpharmaceutical interventions (e.g., masks), performance data on various types of tests, and the nature of the disease. With more information resources can be diverted to the most impactful interventions or technologies.

    b. Document the costs of services and commodities. This will ensure that actual costs and use of resources are measured for future budgeting and resource allocation.

The IMF also provides a guide on options for mitigating corruption risk as flexible and accelerated spending measures are introduced. Important considerations include:

1. Ensure that adequate guidelines accompanying emergency response spending. In South Africa, a National Treasury Instruction created exceptional procurement processes that facilitate procurement of identified items at prenegotiated prices, ensuring security of supply and preventing deviation from established guidelines.
2. Centralize procurement with a partner oversight agency. South Africa's National Treasury provides oversight to the procurement agency to ensure compliance, appropriate spending of resources, and monitoring of costs
3. Share information and ensure transparency. Rwanda publishes hospital procurement data, and Ukraine created a module to monitor detailed procurement information in its e-procurement catalog.
4. Invest and leverage financial management information systems (FMIS). Many countries have implemented FMIS in which modules can be created to monitor resources for the pandemic and flag any deviations.
5. Strengthen processes by ensuring invoices are provided, transactions are recorded, proof of receipt of goods is provided for payment authorization, and frequent audits are conducted. During the Ebola crisis, Liberia increased the frequency of audits of its National Ebola Trust Fund to every quarter.
6. Try electronic fund transfer mechanisms that are easy to monitor and follow up.

Finally, many countries are providing incentives for health care workers and frontline workers or increasing the number of workers who should be taken into consideration. Ghana has lifted payroll taxes and is providing additional compensation. Other countries, including the Philippines or India (State of Kerala), are encouraging returning expatriate health care workers to rejoin the workforce.

8.1 Costing

A robust budget will need to be supported by methodical costing of inputs, future scenarios, and contingencies. The WHO Regional Office for Europe launched the Better Labs for Better Health initiative in 2012 and created a laboratory test costing tool that tracks laboratory expenditures and the actual cost of tests. The spreadsheet-based micro-costing tool includes equipment, reagent, facility, personnel, and quality management cost worksheets where data on costs can be entered to calculate the costs for tests. This could be an effective tool for supporting budgeting and policy formulation for laboratory testing. However, it may not be a practical tool for initial stages or high-intensity stages of the pandemic, since it requires a certain level of effort. In such cases, LMICs may need to adopt a more practical and assumption-based approach. Gross-costing or top-down costing approaches, which usually rely on large, aggregated national data and secondary data, may be a more feasible approach. Therefore, data on number of cases and modeling of future estimates of cases, use estimates for testing commodities and human resources, and other inputs can be used with a gross-costing approach for budgeting.

8.2 Scenario Modeling

The budgeting and financing of testing will be contingent on the disease epidemiology of each country and the interventions carried out to curb the epidemic. While every country will have a unique trajectory, there are various scenario-modeling tools that have been or are under development. Imperial College London has an online tool that provides the future scenarios of Covid-19 burden for LMICs (https://mrc-ide.github.io/global-lmic-reports/) and an additional simulation tool that provides projections for prevalence of infections each day (https://www.covidsim.org/). Both tools provide scenarios based on inputs regarding various types of interventions undertaken and the success/compliance of the interventions. Africa CDC has also developed its own modeling tool for the region, which can be accessed by contacting the team directly. The Center for Disease Dynamics and Economic Policies also offers a modeling tool for Africa and projections for individual countries based on interventions (https://cddep.org/publications/modeling-Covid-19-transmission-in-africa/). Countries have developed their own models and projections (e.g., South Africa), which should be the long-term goal for most countries. Country-specific tools can consider their own context and granular plans to provide for more robust estimates. The Covid-19 Multi-model Comparison Collaboration (CMCC), established by multiple stakeholders to support LMICs in their scenario-modeling efforts, provides a comparison of the key models being used by various global actors and countries. The CMCC literature review reveals 31 models for predictions related to Covid-19 diagnosis and prognosis. The initial two reports and comparison of the seven most-used models provides an overview of the main models, expected outputs, and limitations. This will help countries choose the appropriate model for their current and future needs.

9. Conclusions and Recommendations

The increasing demand for Covid-19 diagnostic tests present several challenges to already-stretched LMICs health systems. The global demand for diagnostics, reagents, and consumables for Covid-19 has led to shortages of commodities even as Covid-19 disrupts global supply chains and economies. In response to the rapidly growing need and the shortage of tests and reagents, several diagnostic test manufacturers around the world have committed to developing and supplying rapid test kits to detect the SARS-CoV-2 virus. Currently, several hundreds of tests are available in the global market; however, only some have received EUA approval from stringent regulatory authorities (e.g., 203 had US FDA EUA approval as of the first week of August). From the present analysis, a few observations can be made:

- All countries face challenges in scaling up testing due to the finite supplies for tests and testing capacities. Given these limitations, countries have had to make some practical choices that may not adhere to the recommended guidelines from international guiding bodies such as WHO. Despite limitations, antigen tests are being used for large-scale testing because access to molecular tests is limited. While this strategy may not be the most efficient, it is still helpful in identifying infected individuals rather than using the gold standard of molecular testing.
- All countries need to persistently monitor the pipeline of diagnostics being introduced into the market as well as the validation of products already introduced. This will help enable quick course correction in the case that low-performing tests are being used widely. This will also help in diversification of suppliers.
- Countries need to use the best available evidence when selecting diagnostics for Covid-19. Simplified application of test selection frameworks such as HTA or ASSURED is important. Using rapid reviews within the context of these frameworks will allow for informed choices for selection of tests for the country. The evidence and evaluation process can be strengthened as new evidence on Covid-19 and testing emerges. Short-term and medium-term pandemic management and testing strategies can regularly be updated if an evidence-based framework already exists. Evidence-based assessments found at repositories of global HTA networks such as Health Technology Assessment International (available at **https://htai.org/hta-support-for-Covid-19/online-resources/**) provide high-quality and useful information that LMICs can leverage.
- Countries need to actively engage with global and regional collaboration initiatives such as Accelerator Covid-19 Tools, Pandemic Action Network, and Partnership to Accelerate Covid-19 Testing in Africa. This will not only allow for visibility into the diagnostics pipeline, but will also help leverage the pooled procurement mechanisms linked with these initiatives.
- Countries should consider value-based pricing mechanisms for procurement of tests and supplies. Information on real world performance of Covid-19 diagnostics is limited. Strong monitoring of the effectiveness of tests being deployed will help policy makers to go back to the table and negotiate with suppliers.
- Regulatory systems and frameworks in LMICs and high-income countries can facilitate manufacture, approval, distribution, access to, and use of much-needed diagnostic equipment, tests, and reagents. Many stringent regulatory authorities, such as the FDA and the European Medicines Agency, have used regulatory tools such emergency use authorization. The tools have expedited approval to use Covid-19 tests and equipment. It behooves NRAs in LMICs to undertake the relevant regulatory adaptations to expedite access to and use of much-needed diagnostic equipment and tests. Several supportive initiatives, such as the AMDF and WHO EUL, have also

been introduced to facilitate market access and entry of novel diagnostics in LMICs. NRAs must endeavor to set quality assurance guidance and requirements in relation to the selection and procurement of Covid-19 POC, near-POC, and laboratory diagnostic technology.

- Supply chain bottlenecks can also impede access to and use of approved diagnostics. Identifying and implementing strategies to mitigate these bottlenecks at the global, national, facility, and last-mile levels is critical. Strategic use of information systems, networks, and pooled logistics practices during pandemics such Covid-19 will help assure access to raw materials and maintain good visibility on shipment items and volumes. Another look at the need to develop open-systems diagnostic equipment platforms to enable multisourcing of cartridges, as well as chemicals for diagnostics, may enable LMICs to access much-needed cartridges and reagents during crises such as the current Covid-19 pandemic.
- At the onset of pandemics, LMICs should analyze and use epidemiological data, seropositivity data, and morbidity data effectively. This data can be used to assess the target potential in need and the quantities of tests kits needed. Understanding and maintaining visibility on testing capacity at all times will enable LMICs to determine testing needs at all times. Following that, LMICs need to improve data infrastructure and reporting, and expand the use of data to drive performance and improve decision making, especially for quantification and forecasting of tests for their populations.

This document and analysis are supported by an open-source dashboard that provides updated information for end users and policy makers on quality-assured Covid-19 diagnostics. The Covid-19 technologies pipeline, knowledge of the virus, and impact of various pandemic management strategies is still evolving. There is a need for continual technical review and updating of considerations and strategies as new knowledge emerges.

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